

REMARKS

I. Detailed Action

Claims 1-4, 9-14, 16-22, 24, 36 and 38-39 are pending.

II. Drawings

The Examiner states Figures 4 and 5 remain objected to because they are undecipherable.

Applicants are submitting separately black and white photographs of Figures 4 and 5. The

Applicants are currently attempting to obtain color photographs.

III. Claim Rejections-35 U.S.C. § 112

Claim 4 stands rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the claimed invention.

The Applicants have amended claim 4 to recite gramineae species. In the Applicants' March 25, 2003 response, support and evidence is provided for the effectiveness of overexpression of betaine dehydrogenase and choline monooxygenase in gramineae species plants. A person skilled in the art of plant transgenics at the time the application was filed would be familiar with the techniques involved in generating a plant that expresses a gene involved in betaine synthesis under the control of a low temperature promoter. Moreover, the description clearly demonstrates that by increasing the concentration of betaine or derivative thereof in a plant provides an increase in cold or freezing tolerance in a plant (for example, on page 10 starting at line 17 and at page 8 beginning at line 9).

IV. Claim Rejections-35 U.S.C. § 103

Claims 1-3, 9-14, 16-20, 21-22, 24, 36, 38 and 39 were rejected under 35 USC § 103(a).

The Examiner has alleged that the invention is prima facie obvious on the basis of cited art involving betaine research, including the following: Rajashekar, regarding strawberry plants, Kishitani, regarding barley plants, and Zhao regarding alfalfa¹. However, the Examiner has also alleged that the effect of betaine accumulation in plants is highly unpredictable².

The Applicants respectfully note that the Examiner has not reconciled these two apparently contradictory positions. The Applicants respectfully submit that their claims for rosacea and gramineae are not obvious in view of the cited art involving experiments with other species of plants. The Examiner has not established a prima facie case by combining Rajashekar, Kishitani and Zhao which were cited in respect of three different types of experiments in different plant species. One could not predict the dramatic results of combination of betaines and cold acclimation from this art or any other art cited by the Examiner.

¹ In paragraphs 34-42 of the September 25, 2001 Office Action, the Examiner cites Rajashekar, regarding strawberry plants, Kishitani, regarding barley plants, and Zhao regarding alfalfa and states that "it would have been prima facie obvious to one skilled in the art that the time that the invention was made to combine cold acclimation and the exogenous administration of betaine to a plant for the purpose of increasing or inducing cold or freezing tolerance in a plant without any surprising or unexpected results. In addition, specific lethal temperature and acclimation temperatures would be unique to the species and cultivars used, and thus would represent alterations of design parameters that would have been obvious to one of ordinary skill in the art at the time the invention was made. The timing of the administration of betaine, the administration of betaine compositions other than glycine betaine, and the concentration of betaine administered would also represent obvious alterations of design parameters."

On page 10 of the August 13, 2002 Office Action, the Examiner states that "the combined treatment of exogenous betaine and cold acclimation would be expected to increase cold tolerance over the plant's normal genotypic potential, because one skilled in the art would recognize that the application of exogenous betaine would allow for accumulation of higher concentrations of betaine than the plant would be able to synthesize in response to cold acclimation alone, and because one skilled in the art would also recognize that many physiological changes other than betaine accumulation are known to occur as a consequence of cold acclimation."

² In the Sept. 25, 2001 Office Action, in relation to claims directed to methods for increasing cold or freezing tolerance in plants, the Examiner alleged that the Applicants have not enabled the invention because "Guidance for making and using the invention is necessary for enablement because the effect of betaine accumulation in plants is highly unpredictable" (page 7, par. 20). In the same Office Action, at paragraph 23, the Examiner stated that "Because different plant species may respond differently to the application and accumulation of glycine betaine, the effect of betaine accumulation in plants is highly unpredictable."

The Examiner has also provided no evidence for the position on page 9 of the outstanding Office Action that "increased cold or freezing tolerance at the leaf level is indicative of a significant increase at the whole plant level, as the leaf is a significant portion of the whole plant in many plant species, and because the leaf is an organ that is ordinarily susceptible to the detrimental effects of cold or freezing temperatures." The Applicants disagree with this statement and request that the Examiner provide evidence for this position, otherwise it is submitted that a prima facie case of obviousness has not been established based on the cited art. In certain cases, leaf shows a significant resistance to freezing while roots do not show the same degree of tolerance, hence when the whole plant is exposed to freezing, it does not survive due to the sensitivity of the roots. It is important to note that the leaf is not the only important part of the plant. In other plants, the whole aerial part dies and the plant still survives due to the survival of apical meristems.

In order to expedite prosecution, the Applicants have proposed a reasonable scope of claim based on the teachings in the application. The application shows drastically increased freezing tolerance of wheat, barley and turf (e.g., page 7, line 10 to page 8, line 16; page 8, lines 19-22 and legends for figures 4-5). Such an improvement is not taught in the prior art. Detailed submissions on this issue are provided in detail in the Applicants' prior response. The claimed methods are enabled for the claimed plants, rosacea and gramineae. Clear guidance for using the method of the invention with these plants is found on page 8, lines 25-31. A skilled person in possession of these teachings would be able to use the methods of the invention with rosacea and gramineae. Thus, the pending claims are enabled by the application and they are not obvious in view of the prior art.

We briefly reemphasize the invention and some of its strong support. The invention shows the dramatic results obtained by the combined effect of betaine and cold acclimation to provide a greater tolerance to freezing and to other stress. The finding that one could increase tolerance above the known genotypic capacity to acclimate was both surprising and unexpected.

Applicants strongly assert that the cited references do not teach, nor suggest, the claimed unique invention. In a wheat example, it is stated on page 3, lines 21-25 that the LT50 for cold acclimated wheat not treated with betaines is -8 degrees C. The LT50 for wheat treated with betaines alone is -8 degrees C. However, the LT50 of wheat treated with betaines in combination with cold acclimation is -14 degrees C. This 6 degree change is very large and unexpected. It is 75% more below the freezing temperature than the results obtained with cold acclimation alone or betaines alone. Figure 1a and 1b persuasively show this result. Plant survival is increased **5-6 fold** compared to untreated plants (page 7, line 38 to page 8, line 1). There is clearly a synergistic effect from the combination of betaines and cold acclimation. One skilled in the art would not predict that such a dramatic increase in freezing tolerance could be obtained.

This synergy was not predictable in part because the interaction of betaines and cold acclimation was not known or understood prior to this invention. The application provides certainty on the mechanism of action of betaines and cold acclimation in order to increase freezing tolerance. The inventors showed that WCOR410 is increased as a result of the combination of betaines and cold acclimation. The inventors also showed that the increased freezing tolerance was not due to other properties of betaines. For example, betaine is an osmolyte, however treatments with other osmolytes (NaCl and mannitol; page 9, lines 4-7) allowed the osmolality to increase as much as betaine, but freezing tolerance was not

significantly improved. The Applicants have shown not only the surprisingly strong result from the combination of betaines and cold acclimation, but they have provided a rational basis to explain the effects of the combination of betaines and cold acclimation.

In response to the rejection of claim 36 on page 7 as indefinite for use of the phrase "about an optimal cold or freezing tolerance", the Applicants have cancelled claim 36.

In response to the rejection of "grass plant" and "graminease species" in claims 1 and 24 as indefinite, the Applicants have amended these claims to delete "grass plant."

In response to the indefiniteness rejection of claim 1 for reciting "nontoxic concentration", the Applicants submit that the meaning of this term is clear to a person skilled in the art. However, the Applicants have more precisely defined this term by stating "the concentration being non-toxic wherein chlorosis does not occur in the plant."

Support for the amendments made to claim 1 is found on page 7, lines 27-30 and page 8, lines 28-31. Support for the amendment made to claim 22 is found on page 8, lines 11-16 and page 9, lines 5-9.

V. Conclusion

For the foregoing reasons, it is respectfully submitted that the proposed amendments be entered, and with their entry, the application is now in condition for allowance.

No fees or extensions of time are believed to be due in connection with this amendment; however, consider this a request for any extension inadvertently omitted, and charge any additional fees to Deposit Account No. 26-0084.

Reconsideration and allowance is respectfully requested.

Respectfully submitted,



Heidi S. Nebel, Reg. No. 37,719
McKEE, VOORHEES & SEASE, P.L.C.
801 Grand Avenue, Suite 3200
Des Moines, Iowa 50309-2721
Phone No. (515) 288-3667
Fax No. (515) 288-1338
CUSTOMER NO: 22885

Attorneys of Record

RECEIVED

JUL 09 2003

OFFICE OF PETITIONS